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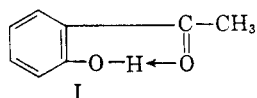
Reactions with Diazoalkanes. VII. Action of Diazomethane on *o*-Hydroxychalkones

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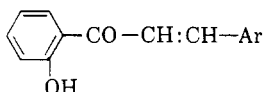
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Phenolic hydroxyl groups ortho to a carbonyl group frequently exhibit abnormal behavior which is ascribed to intramolecular hydrogen bonding. Failure to react with diazomethane under normal conditions is a well known example. This is of diagnostic value in establishing the structure of hydroxy-anthraquinones, -flavones, -xanthenes, and *o*-hydroxyanis. ¹⁻⁷

The generally accepted reason ^{8,9} for the stability of ortho phenolic hydroxyl groups and related substances toward diazomethane is the formation of a chelate ring system, *e.g.*, I in the case of *o*-hydroxyacetophenone. ³



We now have examined the behavior of a number of *o*-hydroxy-substituted chalkones having the phenolic hydroxyl group ortho to the carbonyl group (IIa-i) toward the action of ethereal diazomethane solution.



- IIa. Ar = C₆H₅
 b. Ar = C₆H₄-CH₃(*p*)
 c. Ar = C₆H₄-OCH₃(*o*)
 d. Ar = C₆H₄-OCH₃(*p*)
 e. Ar = C₆H₄-N(CH₃)₂(*p*)
 f. Ar = C₆H₃:O₂:CH₂ (3:4)
 g. Ar = C₆H₃(OCH₃)₂ (3:4)
 h. Ar = C₆H₄-Cl (*o*)
 i. Ar = C₆H₃(OH)(Cl) (2:5)

The reactivity of the α , β -unsaturated bond in α , β -unsaturated esters and ketones (*cf.* benzalacetophenone) toward the action of diazomethane to give pyrazoline derivatives (*cf.* Scheme A) has been thoroughly investigated. ¹⁰⁻¹⁵

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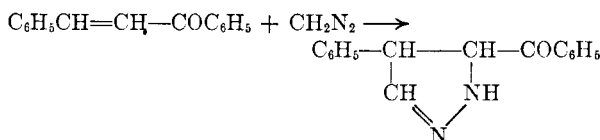
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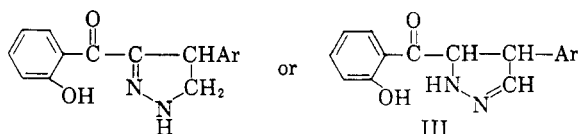
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Scheme A

The phenolic hydroxyl groups of (IIa-i) have failed to react with diazomethane under normal conditions, even after prolonged contact. At low temperature no methylation occurred, thus showing the abnormal behavior of such groups ortho to a carbonyl group which is ascribed to chelation.



The analytical results are concordant with the values corresponding to addition of one molecule of diazomethane. Treatment of (IIa-i) with ethereal diazomethane in presence of methanol does not effect methylation of the hydroxyl group ortho to the carbonyl group. ¹⁶

On the other hand, treatment of (IIIi) with ethereal diazomethane under normal conditions effects the methylation of the hydroxyl group not in an ortho position to the carbonyl group, as well as addition to the α , β -unsaturated bond to form the pyrazoline derivative [IIIi, Ar = C₆H₃(OCH₃)Cl(2:5)]. The latter gives color reaction with ferric chloride, showing the presence of a free phenolic hydroxyl group, most probably that ortho to the carbonyl group.

The pyrazoline derivatives are assigned the structure (III), in favor of which is the fact that

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(16) *Cf.* the finding that methylation of a number of *o*-hydroxyketones could be rendered possible with ethereal diazomethane in presence of methanol. ^{2,3,5}

TABLE I
 Δ²-PYRAZOLINE DERIVATIVES

Start- ing Mate- rial	Prod- uct	Sol- vent ^a	M.p., °C.	Yield, %	Formula	Carbon, %		Hydrogen, %		Nitrogen, %		Chlorine, %	
						Calcd.	Found	Calcd.	Found	Calcd.	Found	Calcd.	Found
IIa	IIIa	A	188-189	68	C ₁₆ H ₁₄ N ₂ O ₂	71.09	71.90	5.46	5.37	10.94	10.72		
IIb	IIIb	B	162-163	85	C ₁₇ H ₁₆ N ₂ O ₂	72.85	72.72	5.71	5.95	10.0	9.85		
IIc	IIIc ^b		130	65	C ₁₇ H ₁₆ N ₂ O ₃	68.91	68.85	5.40	5.33	9.45	9.51		
IIc	IIIc		130	65	C ₁₇ H ₁₆ N ₂ O ₃	68.91	68.69	5.40	5.41	9.45	9.50		
IIe	IIIe	D	157-158	69	C ₁₆ H ₁₃ N ₂ O ₂ Cl							11.81	11.65
IIc	IIIc		130	65	C ₁₇ H ₁₆ N ₂ O ₃	68.91	68.69	5.40	5.41	9.45	9.50		
IIf	IIIf	D	172-173	78	C ₁₈ H ₁₅ N ₂ O ₂	69.90	69.13	6.14	6.40	13.59	13.32		
IIg	IIIg	E	146-147	70	C ₁₇ H ₁₄ N ₂ O ₄	65.80	66.04	4.51	4.65	9.03	8.89		
IIh	IIIh	D	65-66	70	C ₁₈ H ₁₈ N ₂ O ₄	66.25	66.24	5.52	5.60	8.58	8.30		
IIi	IIIi ^b		80	70	C ₁₇ H ₁₅ N ₂ O ₃ Cl	61.71	61.21	4.53	4.60	8.47	8.68	10.74	10.45

IIa, W. Feuerstein and St. V. Kostanecki, *Ber.*, **31**, 715 (1898); IIc, J. Tambor and Hans Gulber, *Chem. Zentr.*, **I**, 737 (1919); IId, F. Herstein and St. V. Kostanecki, *Ber.*, **32**, 318 (1899); IIe, H. Nageli and J. Tambor, *Chem. Zentr.*, **I**, 2366 (1924); IIf and IIg, H. Ozawa, T. Okuda, M. Kawanishi, and K. Fujji, *J. Pharm. Soc. Japan*, **71**, 1178 (1951); *cf. Chem. Abstr.*, 6124 (1952); IIh, A. Rothlisberger, *C. I.*, 2226 (1925).

IIb and IIIi were prepared as follows: A solution of one mole of *o*-hydroxyacetophenone and one mole of the aldehyde (*p*-tolualdehyde or 2-hydroxy-5-chlorobenzaldehyde) in ethanol was treated with 50% sodium hydroxide solution. The reaction mixture was heated 1 hr. (50° bath temperature). It was left for 48 hr. and the sodium salt that separated was acidified with dilute hydrochloric acid, and crystallized.

IIb (90%) crystallized from ethanol as yellow crystals, m.p. 71°.

Anal. Calcd. for C₁₆H₁₄O₂: C, 80.67; H, 5.88. Found: C, 80.09; H, 5.74.

IIIi (85%) was crystallized from benzene in shining plates, m.p. 198-199°.

Anal. Calcd. for C₁₅H₁₁O₃Cl: C, 65.57; H, 4.00; Cl, 12.93. Found: C, 65.61; H, 3.98; Cl, 12.91.

^a A = ethanol; B = dilute ethanol; C = methanol; D = benzene-light petroleum (b.p. 50-70°); E = benzene.

Active hydrogen of IIIa: Calcd. for one active hydrogen, 25%; for two active hydrogens, 50%. Found: 33%. This value may correspond to a free active hydrogen atom and a bonding hydrogen atom.

^b Recrystallization of the crystalline reaction product gave yellow oil from which no crystalline material could be separated.

Δ¹-pyrazolines rearrange very readily to give Δ²-pyrazolines (*cf.* the ready rearrangement Δ¹-3,4-dibenzoylpyrazoline and Δ¹-3-aceto-4 phenylpyrazoline). Such rearrangements have been occasionally reported and are even effected by repeated crystallization or even by effect of glassware.¹³⁻¹⁵ When pyrolyzed, the Δ²-pyrazolines (IIIa and IIIc) give largely dark tars from which we have not succeeded to isolate crystalline products. The Δ²-pyrazolines were stable in air, and could be stored for several months without decomposition. When (IIIb) was allowed to react with phenyl isocyanate, no reaction could be reported under the given experimental conditions, and the starting material was recovered almost completely. The decomposition of the pyrazolines is under further investigation.

EXPERIMENTAL

Action of diazomethane on the chalkones (IIa-i). A solution of 1 g. of each of (IIa-i) in ether (*ca.* 50 ml.) or benzene-ether

mixture was treated with ethereal diazomethane solution (from 5 g. of nitrosomethylurea). The reaction mixture was kept at 0° for 48 hr., during which fresh amounts of diazomethane were added. The reaction products were washed with cold light petroleum (b.p. 40-60°) several times and crystallized. The pyrazoline derivatives (IIIa-i) are yellow crystals which dissolve in aqueous sodium hydroxide solution; their alcoholic solutions give violet color with alcoholic ferric chloride and red color with cold concentrated sulfuric acid. The products are listed in the following table:

Action of diazomethane in presence of methanol on chalkones. The previous experiments were repeated on (IIa-i) and in each case 5 ml. of methanol were added. Similar are obtained as mentioned above.

Action of phenyl isocyanate on IIIb. One gram of the pyrazoline was heated with 0.85 g. of phenyl isocyanate on the steam bath for 3 hr. Methanol (30 ml.) was added to destroy excess phenyl isocyanate, the yellow solution was diluted with water, and the precipitate obtained proved to be unchanged pyrazoline (m.p. and mixed m.p.).

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